ication costs were not statistically different between two groups. Factor positively associated with service costs included excess filler (RR=7.9, p<0.0002), relapse event (RR=4.0, p<0.0001) and adverse event like EPS (RR=1.6, p<0.008), while types of antipsychotics and diagnoses were not significant factors after adjusting for covariates. **CONCLUSIONS:** SGAs were associated with reduced psychiatric service uses as compared to FGAs within the 12-month treatment period; however, service costs were not different and medication costs were significantly higher in the SGAs group. Excess fillers, relapse and incidence of EPS were factors of high costs among children and adolescents psychiatric patients treated with antipsychotics in Taiwan.

PIH49

POPULATION ACCESS TO ROTAVIRUS VACCINATION IN DEVELOPPED COUNTRIES: LESSONS LEARNED FROM CURRENT EXPERIENCE AND POTENTIAL IMPLICATIONS FOR THE FUTURE

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OBJECTIVES: In developed countries, rotavirus disease causes significant burden, both on health care systems and society. Two effective and well-tolerated rotavirus vaccines were marketed in Europe & USA in 2006. Since then, there have been significant discrepancies in policy decisions and health technology assessments (HTAs) relating to the inclusion of universal vaccination into national immunisation programmes, thereby causing unequal population access to rotavirus vaccination. This study aims to understand past HTAs and policy decisions concerning the recommendation, funding and implementation of universal rotavirus vaccination in developed countries. **METHODS:** A comprehensive literature search and critical appraisal of rotavirus HTAs, statements and policy decisions was performed in 20 developed countries (17 Western European countries, USA, Canada and Australia). **RESULTS:** Rotavirus HTAs/statements have been issued in 15 out of 20 countries included in this study. At mid-June 2012, 8 countries have implemented rotavirus vaccination programmes; 2 countries have not recommended vaccination; 2 countries have recommended and funding processes are ongoing. In all other countries, the rotavirus decision-making process has not started or is underway. Despite significant differences in HTA criteria, methods and processes across countries, there is consistency in the key parameters impacting policy decisions: burden of disease, economic evaluation, vaccine efficacy and safety. Positive or negative outcomes largely depend on varying interpretations of similar evidence. For example, several National Immunisation Technical Advisory Groups and policy makers considered evidence pertaining to rotavirus disease burden (morbidity) as significant enough to justify its inclusion in the national immunisation programme, whereas others considered it as insufficient since rotavirus mortality is low. **CONCLUSIONS:** This study highlights the need for a common decision analytic framework to foster structured and transparent HTAs and improved decision-making processes, with the ultimate aim of enhancing future European population access to rotavirus vaccination.

PIH50

TRENDS IN POST-MARKETING COMMITMENTS RELATED TO PREGNANCY AND LACTATION

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OBJECTIVES: Five years ago the United States government passed the Food and Drug Administration Amendments Act of 2007 (FDAAA) expanding the FDA's authority to require post-marketing studies. Prior to this, pregnancy registries, a valuable tool for studying the teratogenicity of newly marketed drugs, were primarily voluntary efforts. Both the FDA (2002) and EMA (2005) issued guidance on post-marketing studies during pregnancy. The objectives of this research were to evaluate the impact of FDAAA on childbearing populations and trends in post-marketing commitments/requirements (PMC/Rs). **METHODS:** Publicly available FDA databases were analyzed to identify all new molecular entities approved between January 2008 and May 2012 and associated PMC/Rs and REMS related to pregnancy/lactation in humans. Data was augmented from the FDA's list of pregnancy registries and assigned pregnancy drug category. **RESULTS:** Over the 4.5 year period, the FDA approved 125 new compounds (100 drugs, 25 biologics). Overall 78% had at least one PMC/R (79% of drugs, 84% of biologics). The proportion of new drugs with a pregnancy related PMC/R was 9% overall and increased over time from 5% in 2008 to a peak of 19% in 2010 before declining to 4% in 2011. Pregnancy categories were B (26), C (70), D (17), X (12). Of the 57 pregnancy registries listed on the FDA's website, 13 are associated with drugs approved during the time period under study however only 6 of these were PMC/R and all were for category C compounds. A single category X drug had a pregnancy/lactation related PMC/R. **CONCLUSIONS:** The majority of pregnancy registries are for medicines with FDA assigned pregnancy category C. Category X drugs are not more likely to have REMS or PMC/Rs despite their known potential for reproductive harm. Population characteristics such as gender, age, and indication for the prescription are powerful indicators of when PMC/Rs are necessary.

PIH51

REVIEW OF ALL PRODUCTS AUTHORIZED BY THE EUROPEAN MEDICINES AGENCY FROM 1995 TO 2011 IN REGARD TO PEDIATRIC INVESTIGATION PLAN APPLICATIONS

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OBJECTIVES: Pediatric Investigation Plans (PIPs) were introduced by the European Commission in January 2007 to help ensure that medicines for children are included in the mainstream drug development process in Europe. The objective of this study was to review all authorized products by the European Medicines Agency (EMA) from 1995 to 2011 to identify (1) products with a potential pediatric indication, and (2) products with a PIP application. **METHODS:** On the EMA website, the European Public Assessment Reports (EPARs) were searched manually. For each product, the Summary of Product Characteristics (SmPC) was reviewed to explore quotes relative to any potential pediatric indication. The products were distributed in four categories: C1=adult indication only; C2=safety/efficacy not studied in children; C3=adult and pediatric indication; and C4=pediatric indication only. For each product, the EMA pediatrics database was searched for PIP applications. **RESULTS:** A total of 633 products were authorized by the EMA (281 in 1995-2006 and 352 in 2007-2011). From 1995 to 2006, 33.53% of the authorized products presented a lack of evidence in the pediatric population as did 57% in the period of 2007-2011. In total, 746 PIP applications were identified (products authorized and under development). A PIP was requested for 21.4% of the products authorized before the regulation (1995-2006) and for 19% of the products authorized after the EU pediatric regulation. **CONCLUSIONS:** The categorization of authorized products according to the SmPC quotes showed that many products had potential pediatric indications needing confirmation through new research programs. As expected, most of the PIP applications concern products under development. However, it is interesting to note that 20% of the requests concern authorized products, with a higher percentage of requests for products authorized before the regulation. These findings suggest that the pediatric regulation in Europe is fostering research to create more therapeutic options for children.

NEUROLOGICAL DISORDERS - Clinical Outcomes Studies

PND1

12-MONTH CLINICAL EVOLUTION OF MODERATE ALZHEIMER'S DISEASE PATIENTS IN SPAIN: THE EVOCOST STUDY

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OBJECTIVES: There is a lack of long-term data from the real-life setting to document the clinical evolution of Alzheimer's disease (AD) patients, especially in moderate AD where disease management becomes more complex. The EVOCOST study aims to describe how moderate AD is associated with a relevant disease-related disability progression and an increase in caregiver burden. **METHODS:** The EVOCOST study is a prospective 12-month multicentre cohort study recruiting community-dwelling moderate AD patients in Spain. Visits were scheduled at baseline, 6 and 12 months according to routine clinical practice. Data on socio-demographic characteristics, disease history and comorbidities were collected at baseline. Clinical evolution and caregiver burden were measured using the following assessment tools: Global Deterioration Scale (GDS) for severity, Mini-Mental State Examination (MMSE) for cognition, Clinical Global Impression (CGI) for global status, Basic and Instrumental Activities of Daily Living (BADL and IADL) for functional disability, brief Neuropsychiatric Inventory (NPI-Q) for behaviour, Zarit Burden Interview (ZBI) and time spent on care for caregiver burden. Changes from baseline were calculated and tested with Wilcoxon signed rank tests. **RESULTS:** A total of 209 patients were included at baseline, 76.1% of them were women, with a mean age of 78.4 years and a mean MMSE of 15.2. At the 12-month visit, data were available on 174 patients (patient's attrition rate 16.8%). Clinical symptoms worsened significantly during the 12-month study follow-up in terms of severity (ΔGDS=+0.5, p<0.001), cognition (ΔMMSE=-2.9, p<0.001), global status (ΔCGI=+0.3, p<0.001), and function (ΔBADL=-1.7, p<0.001; ΔIADL=-1.2, p<0.001). No significant change was observed on behaviour (ΔNPI severity=+0.5, p=0.325; ΔNPI distress=+0.4, p=0.375). Caregiver burden also worsened significantly (ΔZBI=+2.5, p=0.002; Δtime spent on care=+56hours per month, p<0.001). **CONCLUSIONS:** The EVOCOST study illustrates well the patient clinical worsening and the increase in caregiver's burden associated with management of moderate AD.

PND2

EFFECT OF COGNITIVE BEHAVIOURAL THERAPY IN MULTIPLE SCLEROSIS FATIGUE: A SYSTEMATIC REVIEW OF RANDOMISED CONTROLLED TRIALS

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OBJECTIVES: To assess clinical effectiveness of cognitive behavioural therapy (CBT) in patients with multiple sclerosis (MS) fatigue. **METHODS:** Embase® and Cochrane databases were searched up to June 2012 to identify randomised controlled trials published in English evaluating effect of CBT (disseminated by any mode) in patients with MS fatigue. Eligibility of trials was assessed by two reviewers with any discrepancy reconciled by a third, independent reviewer. To compare CBT with other therapies, random-effect meta-analysis was conducted using Stata® (v11.1) on change from baseline to endpoint in fatigue score. **RESULTS:** Four studies of 107 retrieved citations met pre-defined inclusion criteria. Two studies compared CBT to no therapy and one study each compared CBT to relaxation therapy (RT) and supportive-expressive group therapy (SEGP). All studies were well conducted and no significant differences were observed between treatment groups for demographic characteristics. Weighted mean difference (WMD) demonstrated statistically significant reduction for change in fatigue score at 2 months from baseline with CBT versus no therapy (-7.04; p<0.001). When CBT was compared to RT, WMD was -4.29 (p<0.001) at 2 months, -2.74 (p=0.013) at 5 months, and -2.74 (p=0.027) at 8 months indicating that CBT group improved significantly on fatigue than RT group and this improvement was sustained over a period of time. Further,